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EXAMINER	
RAMIREZ, DELIA M	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 01/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,803	CAUET ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- Th MAILING DATE of this communication appears on the cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-33* is/are pending in the application.

4a) Of the above claim(s) *31 and 33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-30 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7/22/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: Abstract

DETAILED ACTION

Status of the Application

Claims 17-33 are pending.

Applicant's election with traverse of Group I, claims 17-30 and 32, drawn to a method for producing hydroxylated and/or acetylated steroids with yeast transformed to express the Cyp7b gene and a yeast cell transformed to express the Cyp7b gene, in a communication filed on 11/12/2003 is acknowledged.

Applicant's traverse is on the ground(s) that unity of invention exists between Groups I and II since claims 27-28 of Group I are directed towards a yeast with varying levels of 17-dehydrogenase activity including zero activity and claim 31 of Group II is drawn to a yeast with zero 17-dehydrogenase activity by inactivation of the yil124w gene. This is not found persuasive for the following reasons. It is noted that only claim 28 is directed to a method which requires a yeast with low or zero 17-dehydrogenase activity. The yeast required to practice the method of claim of 28 also has to express the product of the Cyp7b gene in addition to have low or zero 17-dehydrogenase activity. Since the yeast of claim 31 is not required to express the Cyp7b gene, Groups I and II do not have the same or corresponding technical feature.

Applicants also argue that there is unity of invention regarding Groups I and III since according to Applicants, the method of claim 33 is merely a use for the method of Group I and it uses the steps of claim 17, which is part of Group I. This is not found persuasive for the following reasons. Claim 33 as written is directed to a method for making a medicinal product which comprises the step of making an steroid made by the process of claim 17 (Group I). As written , the medicinal product may or may not contain the steroid made by the process of claim 17, i.e. the steroid may be further modified in additional steps to produce the medicinal product. Thus, the method of claim 33 is not directed to the method of claim 17 wherein the steroid is used in a medicinal product but rather to a method of making a product

which comprises at least the step of preparing the steroid according to the method of claim 17 (Group I). The methods of claims 17 and 33 do not make the same product. In addition, as indicated Paper No. 7, mailed on 10/15/2003, 37 CRF 1.475 does not provide for the inclusion of multiple methods within the main invention. Therefore, Groups I and III do not have unity of invention.

Applicants also submit that the search of all inventions would not impose an undue burden on the Office. While the Examiner is not arguing that the restriction requirement is proper since searching all of the claimed inventions would impose an undue burden on the Office, it is noted that searching the entire application would require patented and non/patented literature as well as class/subclass searches which may not be coextensive, therefore imposing an undue burden on the Office.

The requirement is deemed proper and therefore is made FINAL.

Claims 31 and 33 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Priority

1. This application is the national stage of PCT/FR00/02753 filed on 10/04/2000.

2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in France (99/12410) on 10/5/1999. It is noted, however, that applicant has not filed a certified copy of said application as required by 35 U.S.C. 119(b).

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on 7/22/2002 is acknowledged. Reference WO 99/40203 has not been considered since no English translation has been provided. The remainder of the submission is in compliance with the provisions of 37 CFR 1.97 and is being considered by the Examiner.

Claim Objections

4. Claims 18 and 24 are objected to due to the recitation of "APAT". Abbreviations unless otherwise obvious and/or commonly used in the art, should not be recited in the claims without at least once reciting the entire phrase for which the abbreviation is used. It is suggested that the term acetyl coenzyme A-pregnenolone acetyltransferase be used at least once followed by its abbreviation in parentheses. Appropriate correction is required.

5. Claim 21 is objected to due to the recitation of "steroids which has". It should be replaced with "steroids which have". Appropriate correction is required.

6. Claim 25 is objected to due to the recitation of "yeasts also carry dehydrogenase activity". For clarity, the term should be replaced with "yeasts also produce a dehydrogenase" or "yeasts also produce a protein having dehydrogenase activity". Appropriate correction is required.

7. Claim 30 is objected to due to the recitation of "promoter chosen in the group consisting of". For clarity, it is suggested that the term be replaced with "promoter chosen from the group consisting of". Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 17-30 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claims 17, 30 and 32 (claims 18-29 dependent thereon) are indefinite due to the recitation of "cyp7b". While it is understood that the term "cyp7b" refers to gene nomenclature, it is noted that gene nomenclature is in some instances species specific. Therefore, the use of this nomenclature for genes

encoding proteins of identical function in any organism may not be accurate. As known in the art, genes encoding proteins of identical function in two different organisms may use different designations. For example, the ARO4 gene of Candida albicans encodes a DAHP synthase whereas the E. coli counterpart is the aroF gene. See the abstract of Sousa et al. (Microbiology 148(Pt5):1291-1303). As such, the use of gene terminology which is applicable to some organisms and not to others is confusing since the claims use this gene nomenclature with respect to any organism. It is also noted that cyp7b is also known as hct-1 (Stapleton et al., J. Biol. Chem. 270(50) 29739-29745, 1995; see Abstract) and cyp7b1 (Wu et al., J. Lipid Research 40:2195-2203, 1999; see Abstract and page 2197, left column, Results, lines 38-41). It is suggested that the term cyp7b be used in conjunction with the name of the protein encoded by it. For examination purposes, it will be assumed that the term "cyp7b gene" is "gene encoding a 7-alpha-hydroxylase which catalyzes 7-alpha hydroxylation of pregnenolone and dehydroepiandrosterone (DHEA)". Correction is required.

11. Claim 20 is indefinite in the recitation of "precursor contains a 7 position..." since it is unclear what a "7 position" is. If the intended meaning is "precursor can be hydroxylated at position 7", the claim should be amended accordingly. For examination purposes, the intended meaning as indicated above will be used. Correction is required.

12. Claim 21 is indefinite in the recitation of "steroids which have a 3-keto function " as it is unclear what a 3-keto function is. For examination purposes, it will be assumed that the term refers to a 3-keto group. Correction is required.

13. Claim 22 is indefinite in the recitation of "said precursor is a steroid with a structure chosen from the group consisting of structures of the androstane....., and stigmastane type" as it is unclear which structures are being recited in the group. As written, one cannot determine whether the precursor must have the same structure as those compounds recited in the claim or if the precursor may share some structural characteristics with the compounds recited. If the precursor can share some structural

characteristics with the compounds recited, it is unclear as to how much structural similarity is encompassed by the claim. For examination purposes, it will be assumed that the intended meaning is "said precursor is an steroid comprising the structure of androstane, androstene, ..., or stigmastane" Correction is required.

14. Claim 24 is indefinite in the recitation of "atf2 gene" for the same reasons indicated above regarding the recitation of "cyp7b". It is suggested that the term "atf2 gene" be used in conjunction with the name of the protein encoded by it, i.e. acetyl coenzyme A-pregnenolone acetyltransferase. For examination purposes, the suggested language will be used. Correction is required.

15. Claims 24 and 28 are indefinite in the recitation of "activity of said yeasts has been rendered low" for the following reasons. The term "low" is a relative term not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. For examination purposes, it will be assumed that the term's intended meaning is "activity ...is lower than that found in wild-type yeasts". Correction is required.

16. Claim 26 is indefinite in the recitation of "wherein said dehydrogenase activity is a 17-dehydrogenase activity which produces a 17-hydroxylated derivative" for the following reasons. It is unclear as to what a "17-dehydrogenase activity" is. For examination purposes, it will be assumed that the term refers to "17 beta hydroxysteroid dehydrogenase activity". In addition, the term "dehydrogenase activity which produces a...derivative" is confusing since it is unclear as to how an activity can produce a derivative. Also, the term "17-hydroxylated derivative" is indefinite since it is unclear as to what a 17-hydroxylated derivative is. For examination purposes, it will be assumed that the claim is directed to the method of claim 25, wherein said dehydrogenase activity is a 17 beta hydroxysteroid dehydrogenase activity and wherein said 17 beta hydroxysteroid dehydrogenase activity catalyzes the production of an steroid precursor hydroxylated at position 17". Correction is required.

17. Claim 27 is indefinite in the recitation of "wherein said ...dehydrogenase activity is carried by the yi1124w gene" for the following reasons. The term "dehydrogenase activity is carried by the ...gene" is indefinite since as known in the art genes can encode a protein with enzymatic activity but genes do not have enzymatic activity. It is suggested that the claim be amended to recite, for example, "wherein said ....dehydrogenase is encoded by ....". In addition, the term "yi1124w gene" is indefinite for the same reasons indicated above regarding the recitation of "cyp7b". It is suggested that if the term "yi1124w gene" is used, the name of the protein encoded by it, i.e. 1-acyl dihydroxyacetone phosphate reductase be also included. For examination purposes, the claim will be interpreted as "the method of claim 26 wherein said 17 beta hydroxysteroid dehydrogenase activity is that of the 1-acyl dihydroxyacetone phosphate reductase encoded by the yi1124w gene". Correction is required.

18. Claim 28 is indefinite in the recitation of "method of claim 17 wherein the 17-dehydrogenase activity...." since there is no antecedent basis for the activity. For examination purposes, it will be assumed that the claim refers to the method of claim 27. Correction is required.

19. Applicants are reminded that when amending the claims in response to this Office Action, care should be taken such that all the examined claims have the proper antecedent basis.

Claim Rejections - 35 USC § 112, First Paragraph

20. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

21. Claims 17-30 and 32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 17, 19-23, 29-30 are directed to a method of making a genus of hydroxylated and/or acetylated steroids using a genus of steroid precursors and a genus of yeasts transformed to produce a genus of 7-alpha-hydroxylases which catalyze 7-alpha hydroxylation of pregnenolone and dehydroepiandrosterone (DHEA). See claim rejections under 35 USC 112, second paragraph for claim interpretation. Claims 18 and 24 are directed to the method of claim 17 with the added limitation that the genus of yeasts produce lower acetyl coenzyme A-pregnenolone acetyltransferase than the wild type yeasts or no acetyl coenzyme A-pregnenolone acetyltransferase. Claim 24 is directed to the method of claim 18 with the added limitation that the reduction or elimination of acetyl coenzyme A-pregnenolone acetyltransferase activity is accomplished by inactivating the corresponding gene or by using a mutant of the corresponding gene. Claim 25 is directed to the method of claim 17 wherein said yeasts also produce a genus of proteins having dehydrogenase activity. Claim 26 is directed to the method of claim 25 wherein the genus of proteins have 17 beta hydroxysteroid dehydrogenase activity. Claim 27 is directed to the method of claim 26 wherein the genus of proteins having 17 beta hydroxysteroid dehydrogenase activity are 1-acyl dihydroxyacetone phosphate reductases. Claim 28 is directed to the method of claim 27 wherein the 17 beta hydroxysteroid dehydrogenase activity in the yeast cells is eliminated or reduced with respect to the wild type yeast cells by any means. Claim 32 is directed to a genus of yeast strains transformed with a genus of genes encoding 7-alpha-hydroxylases which catalyze 7-alpha hydroxylation of pregnenolone and DHEA.

While the specification discloses a method of producing 7 alpha hydroxy DHEA, 3 beta-acetyl DHEA, and 3 beta, 7 alpha, 17 beta androstenetriol from DHEA using S. cerevisiae cells having the S. cerevisiae aft2 gene inactivated by a deletion and transformed with the rat cyp7b gene having the GeneBank's accession number U36992 (Stapleton et al.), the characterization of the S. cerevisiae yil124w gene product, and the construction of mutant S. cerevisiae cells wherein the S. cerevisiae yil124w gene has been inactivated by an insertion, the specification fails to disclose (1) other genes

encoding 7-alpha-hydroxylases which catalyze 7-alpha hydroxylation of pregnenolone and DHEA, (2) other genes from other organisms, including other yeasts, encoding 1-acyl dihydroxyacetone phosphate reductases, (3) other yeast genes encoding acetyl coenzyme A-pregnenolone acetyltransferases (APAT), (4) additional steroid precursors which can be hydroxylated and/or acetylated in the claimed method, (5) other proteins from other organisms having 17 beta hydroxysteroid dehydrogenase activity as well as their corresponding DNAs, (6) other proteins from other organisms having any dehydrogenase activity as well as their corresponding DNAs, and (7) other modifications in any gene encoding any 1-acyl dihydroxyacetone phosphate reductase, any 17 beta hydroxysteroid dehydrogenase, or any acetyl coenzyme A-pregnenolone acetyltransferase which would result in lower expression of those genes when compared to the wild type level of expression or in lower activity of the proteins encoded by those genes, such as mutations in the promoter region or mutations in the coding region. The genus of polynucleotides and steroid precursors encompassed by the claims is a large and variable genus, with the potentiality of encompassing species which are structurally and/or functionally unrelated. Similarly, the genus of modifications which can be made in any gene encoding 1-acyl dihydroxyacetone phosphate reductases, 17 beta hydroxysteroid dehydrogenases, and acetyl coenzyme A-pregnenolone acetyltransferases, such that their expression is reduced or the activity of their products is reduced, is extremely large and variable.

A sufficient written description of a genus of polynucleotides may be achieved by a recitation of a representative number of polynucleotides defined by their nucleotide sequence or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. However, in the instant case, there is no structural feature which is representative of all the members of the genus of polynucleotides required to practice the claimed method and transform the genus of yeast strains claimed. This is also the case regarding the genus of steroid precursors which is required to practice the claimed method since there is no structural feature disclosed which is representative of all the

steroid precursors which can be used in the claimed method. Furthermore, while one could argue that the recited genera of polynucleotides are adequately described by the rat cyp7b gene, the S. cerevisiae atf2, and the S. cerevisiae yi1124w gene, since one could use structural homology using the structures of such genes and those known in the art to isolate other genes as required by the claimed method, it is noted that the art teaches the unpredictability of using structural homology to accurately determine function and even a high degree of structural homology may not result in functional homology. Bork (Genome Research, 10:398-400, 2000) teaches protein function is context dependent, and both molecular and cellular aspects must be considered (page 398). Witkowski et al. (Biochemistry 38:11643-11650, 1999) teaches that one amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β-ketoacyl synthase activity. Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) teaches that two naturally occurring Pseudomonas enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Therefore, in the absence of any additional information correlating structure with function, many structurally unrelated polynucleotides and many structurally and functionally unrelated steroid precursors are encompassed by the claims. The specification only discloses a few species of the genera of genes, steroid precursors, and modifications required to practice the claimed method and transformed the claimed genus of yeast strains, which is insufficient to put one of ordinary skill in the art in possession of all attributes and features of all species within the genera of polynucleotides, precursors and modifications required to practice the claimed method and transform the claimed genus of yeast strains. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

22. Claims 17-30 and 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a yeast cell transformed with the rat cyp7b gene having GenBank's accession

number U36992 (Stapleton et al.) and a method for producing 7 alpha hydroxy DHEA, 3 beta-acetyl DHEA, and 3 beta, 7 alpha, 17 beta androstenetriol from DHEA using S. cerevisiae cells wherein said cells (1) have been transformed with the rat cyp7b gene having GenBank's accession number U36992, (2) have the S. cerevisiae aft2 gene inactivated by a deletion, and (3) have the S. cerevisiae yi1124w gene inactivated by an insertional mutation, does not reasonably provide enablement for (1) a yeast cell transformed with any gene encoding 7-alpha-hydroxylases which catalyze 7-alpha hydroxylation of pregnenolone and DHEA, and (2) a method for producing any hydroxylated and/or acetylated steroid using any precursor and (a) a yeast cell transformed with any gene encoding 7-alpha-hydroxylases which catalyze 7-alpha hydroxylation of pregnenolone and DHEA, (b) a yeast cell transformed with any gene encoding 7-alpha-hydroxylases which catalyze 7-alpha hydroxylation of pregnenolone and DHEA and capable of producing any dehydrogenase from any source, (c) any yeast cell modified in any way such that the gene encoding acetyl coenzyme A-pregnenolone acetyltransferase is expressed at lower levels or its gene product has lower activity when compared to the wild-type yeast, and is also transformed with any gene encoding 7-alpha-hydroxylases which catalyze 7-alpha hydroxylation of pregnenolone and DHEA, or (d) any yeast cell modified in any way such that the gene encoding 1-acyl dihydroxyacetone phosphate reductase is expressed at lower levels or its gene product has lower activity, when compared to the wild type yeast, and is also transformed with any gene encoding 7-alpha-hydroxylases which catalyze 7-alpha hydroxylation of pregnenolone and DHEA. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2nd 1400 (Fed. Cir. 1988) are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6)

the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breath of the claims.

The scope of the claim, as discussed above, is not commensurate with the enablement provided in view of the large number of undisclosed genes, steroid precursors, and modifications required to practice the claimed method and transform the yeast strains claimed. As indicated above, the specification fails to disclose (1)) other genes encoding 7-alpha-hydroxylases which catalyze 7-alpha hydroxylation of pregnenolone and DHEA, (2) other genes from other organisms, including other yeasts, encoding 1-acyl dihydroxyacetone phosphate reductases, (3) other yeast genes encoding acetyl coenzyme A-pregnenolone acetyltransferases (APAT), (4) additional steroid precursors which can be hydroxylated and/or acetylated in the claimed method, (5) other genes from other organisms encoding proteins having 17 beta hydroxysteroid dehydrogenase activity, (6) other genes from other organisms encoding any dehydrogenase, and (7) other modifications in any gene encoding any 1-acyl dihydroxyacetone phosphate reductase, any 17 beta hydroxysteroid dehydrogenase, or any acetyl coenzyme A-pregnenolone acetyltransferase which would result in lower expression of those genes or in lower activity of the gene products when compared to the wild type level of expression, such as mutations in the promoter region or in the coding region. The art as discussed above, clearly teaches the unpredictability of isolating proteins of similar function based solely on structural homology and indicates that even high structural homology does not always result in functional homology. Since structure determines function, one of skill in the art would require some knowledge or guidance as to which are the structural elements in any gene which are characteristic of any gene encoding 7-alpha-hydroxylases which catalyze 7-alpha hydroxylation of pregnenolone and DHEA, 1-acyl dihydroxyacetone phosphate reductases, acetyl coenzyme A-pregnenolone acetyltransferases, 17 beta hydroxysteroid dehydrogenases, or any dehydrogenase, to isolate those genes required by the method and the transformation of the yeast cells claimed. In addition, the specification is silent regarding the many modifications which can be made to a host yeast cell or a

gene as recited in the claim, such that it expresses such gene at levels which are lower than those found in the wild type cell or its corresponding proteins have lower activity. As discussed above, there is no information as to which modifications in the promoter region of a gene can be made to obtain reduced expression nor there is any information as to which mutations can be made to such gene such that the encoded protein has reduced activity, i.e. substitutions, deletions or insertions in the coding region. The only modifications provided by the specification are deletions and insertional mutations to disrupt the recited genes. Moreover, the specification is completely silent as to how one of skill in the art can use any steroid precursor in the claimed method if the enzymes required to produce hydroxylated and/or acetylated steroids are substrate specific.

Therefore, due to the lack of relevant examples, the amount of information provided, the lack of knowledge about the critical structural elements required in any gene to encode proteins having the display the desired function, the lack of knowledge about the structural elements required in any steroid precursor such that it can be used in the claimed method, the lack of information as to which are the modifications which can be made to a yeast cell or a gene such that low expression levels or low activity of the gene product is obtained, and the unpredictability of the prior art in regard to determining the function of a protein based solely on structural homology, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to practice the full scope of the claimed method. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

Conclusion

23. No claim is in condition for allowance.

24. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be

retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
January 15, 2004

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600